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EXAMINER	
VIVLEMORE, TRACY ANN	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,582	HELMLING ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2007 and 28 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,8-14,16-18,20-22,24-27,29-41 and 45-49* is/are pending in the application.

4a) Of the above claim(s) *16-18,20-22,24,25 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8-14,26,27,30-41 and 45-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/8/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *notice to comply*.

DETAILED ACTION

Requirement to comply with sequence rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, figures 13, 19, 22-25 contain sequences lacking identifiers in either the figure itself or in the brief description of the figure. Additionally, page 24 contains both amino acid and nucleotide sequences lacking identifiers.

To be considered fully responsive, any reply to this action must correct these deficiencies, as this requirement will not be held in abeyance.

Election/Restrictions

Applicant's election with traverse of group I, claims 1, 3-14, 26, 27 and 30, in the reply filed on July 23, 2007 is acknowledged. The traversal is on the ground(s) that the nucleotide sequence cited to demonstrate the claims do not make a contribution over the prior art is a primer, and is not the same as the nucleic acid of SEQ ID NO: 33 of the instant application, which is a molecule which binds ghrelin. Based on these assertions applicants conclude the two sequences are unrelated.

This is not found persuasive because the cited sequence meets the structural limitations of the claims, specifically claim 14, which recites that the sequence of claim 8, which includes SEQ ID NO: 33, is from 15-150 nucleotides in length. Since the cited sequence comprises 15 nucleotides of SEQ ID NO: 33 it is considered to meet the structural limitations of the claims and be a nucleic acid that specifically binds ghrelin. Applicants further traverse the restriction to a single nucleotide sequence by arguing that the molecules have a common property of binding ghrelin and assert that they must share a common structure to be able to bind the same molecule. This is not persuasive because applicants have asserted the nucleotide sequence must share a common structure but do not identify what this common structure is.

Applicants further argue that the restriction between groups 1 and 2 should be removed since the search of claim 1 will necessarily encompass the subject matter of claim 2. This is found persuasive and these inventions are rejoined.

The requirement is still deemed proper and is therefore made FINAL.

Claims 16-18, 20-22, 24, 25 and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 23, 2007.

Applicants have canceled claims 5, 7, 15, 19, 23, 28 and 42-44 and added new claims 31-41 and 45-49, which are directed to elected invention. Claims 1-4, 6, 8-14, 26, 27, 30-41 and 45-49 are currently under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specification

The disclosure is objected to because of the following informalities: the specification may not to refer to claims, see page 4. Because claims may be canceled and the final claim numbering would not match the original claims, a reference to claims in the specification is not an adequate description of what is being referred to. It is suggested that the content of any claims referred to in the specification be incorporated into the specification.

Information Disclosure Statement

The information disclosure statement filed May 8, 2007 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most

knowledgeable about the content of the information, of each patent listed that is not in the English language. Therefore, the information referred to in DE 198 08 591 has not been considered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6, 8-14, 26, 30-41 and 45-49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4-10 and 12 of copending Application No. 10/578,938. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to nucleic acids that bind ghrelin while the claims of the '938 application are directed to nucleic acids that bind to bioactive ghrelin. The claims of the two applications differ in that the '938 claims are directed specifically to bioactive ghrelin, however the '938 application defines bioactive ghrelin as ghrelin molecules containing an octanoyl side chain at the third amino acid; a definition identical to that of the ghrelin in the instant specification.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4, 6, 8-14, 26, 27, 30-41 and 45-49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-39, 43-45, 49-51 and 56 of copending Application No. 11/400,459. Although

the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to nucleic acids that bind ghrelin while the claims of the '459 application are directed to nucleic acids that bind to ghrelin and have a particular structure. The '459 claims are an obvious variation of the instant claims because one embodiment of these nucleic acids is SEQ ID NO: 20, which is identical to SEQ ID NO: 8 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

Claims 12, 13 and 31-36 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Each of these claims is directed to a nucleic acid that binds to ghrelin and has a dissociation constant (Kd) between .05nM and 25μM. because the Kd of a particular complex will vary with differing solution conditions such as changes in salt concentration, pH and temperature, in the absence of additional descriptive characteristics any nucleic acids meeting the structural limitations of the claims are considered to have the recited Kd under some combination of solution conditions, therefore these claims do not further limit the claims from which they depend.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 26 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bryant et al. (US 2003/0211967) in view of Gold et al. (US 6,110,900.

The claims are directed to antagonists of ghrelin which are nucleic acids that specifically bind to ghrelin. In specific embodiments the nucleic acids bind L-ghrelin and are present in a composition or a kit. For the purposes of applying art, a kit is considered to be equivalent to a claim to a composition.

Bryant et al. teach that obesity is the strongest risk factor known for type II diabetes mellitus and is a strong risk factor for cardiovascular disease and cancer. This

obesity-induced pathology can be attributed to the strong association with dyslipidemia, hypertension, and insulin resistance. Bryant et al. further teach that administration of ghrelin predominantly leads to fat deposition and that blocking or antagonizing ghrelin action induces energy consumption, primarily from fat stores. Bryant et al. teach a method of treating obesity in a mammal by selectively inhibiting ghrelin activity using a ghrelin neutralizing agent. Bryant et al. teach that ghrelin neutralizing agents are agents such as antibodies that specifically bind ghrelin. Bryant et al. do not teach nucleic acids as ghrelin neutralizing agents.

Gold et al. teach a method of identifying nucleic acid ligands (also called aptamers) by a process of *in vitro* selection and amplification. Targets for nucleic acid ligands (see column 13) include any compound of interest for which a ligand is desired, such as proteins and peptides. Nucleic acid ligands are also referred to as nucleic acid antibodies and Gold et al. teach that nucleic acid ligands can be employed in diagnostics in a manner similar to conventional antibody-based diagnostics. Gold et al. also teach at column 9 that nucleic acid ligands have therapeutic uses as sequestering agents, drug delivery vehicles and modifiers of hormone action, which would require formulation of the nucleic acid ligand as a composition.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce nucleic acid aptamers targeted to ghrelin that specifically bind ghrelin. Based on the teachings of Bryant et al. that targeting of ghrelin provides a treatment of obesity one of ordinary skill in the art would be motivated to make antagonists of this peptide. Based on the teachings of nucleic acid ligands

provided by Gold et al., including the teaching that nucleic acid ligands are equated with antibodies and have therapeutic use, and the teaching of procedures for selecting nucleic acid ligands that are generally applicable to any target, one of ordinary skill in the art would recognize that the production of aptamers to any target is provided through the use of routine techniques that are reasonable expected to provide nucleic acid ligands to any target.

Thus, the invention of claims 1, 2, 26 and 30 would have been obvious, as a whole, at the time the invention was made.

Claims 1-4, 6, 26, 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bryant et al. and Gold et al. as applied to claims 1, 2, 26 and 30 above, and further in view of Klussmann et al. (Nature Biotechnology 1996) and Nolte et al. (Nature Biotechnology 1996).

Claims 1, 2, 26 and 30 are described in the previous rejection. Claims 3, 4 and 6 recite that the nucleic acid comprises at least one L-nucleotide or is able to bind L-ghrelin.

The teachings of Bryant et al. and Gold et al. are described in the previous rejection. Neither of these references teaches the use of L-nucleotides or the binding of a target comprising L-amino acids.

Klussmann et al. teach that a limitation of the therapeutic use of nucleic acids is the rapid nucleolytic degradation in bodily fluids. Klussmann et al. teach that one way to address this shortcoming is the use of modified nucleotides compatible with

conventional *in vitro* selection methods and present an alternative method: the synthesis of aptamers comprised of L-nucleic acids, termed spiegelmers. Klussmann et al. exemplify this concept by producing spiegelmers to recognize adenosine. The teachings of Nolte et al. parallel those of Klussmann et al. and demonstrate the broad applicability of spiegelmers by producing spiegelmers capable of recognizing arginine and a short peptide motif from HIV-1 Tat protein. Both Klussmann et al. and Nolte et al. teach that spiegelmers have affinity and specificity equivalent to the natural D-nucleic acids and have the advantage of not being degraded by intracellular nucleases.

The teachings of Bryant et al. and Gold et al. are obvious for the reasons set forth in the previous rejection. It would have been further obvious to one of ordinary skill in the art to make aptamers targeted to ghrelin as a spiegelmer as taught by each of Klussmann et al. and Nolte et al. One of ordinary skill in the art would be motivated to substitute a spiegelmer for an aptamer because both Klussmann et al. and Nolte et al. teach that spiegelmers have affinity and specificity equivalent to a normal aptamer but exhibit high resistance to nuclease degradation. One of ordinary skill in the art would have had a reasonable expectation of success in producing a spiegelmer targeted to ghrelin because Nolte et al. and Klussmann et al. teach the synthesis of spiegelmers using routine synthetic methods.

Thus, the invention of claims 1-4, 6, 26 and 30 would have been obvious, as a whole, at the time the invention was made.

Allowable Subject Matter

SEQ ID NO: 8 is free of the prior art searched.

Claims 8-11, 14, 27, 37-41 and 45-49 are objected to for containing non-elected subject matter but would be allowable if this non-elected subject matter is removed and the provisional double patenting rejections are overcome.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

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